Results from the largest GWAS of lifetime cannabis use (N=184,765): new risk loci, genetic overlap with mental health, and a causal influence of schizophrenia on cannabis use


Abstract

Cannabis use is a heritable trait that has been associated with adverse mental health outcomes. To identify genetic risk variants, we performed the largest genome-wide association study for lifetime cannabis use (N=184,765) to date. We identified 8 independent SNPs in 6 regions, with all measured variants combined explaining 11% of the variance. Gene-based tests revealed 35 significant genes in 16 regions and S-PrediXcan analyses identified 21 genes with different expression levels between cannabis users versus non-users. The most significant and consistent finding over the different analyses was CADM2, which has previously associated with substance use and risk-taking phenotypes. Significant genetic correlations were found with 14 of 25 tested substance use and mental health traits, including smoking, alcohol use, risk-taking, schizophrenia, and bipolar disorder.

*Shared first author

†Shared last author
Mendelian randomisation analysis provided evidence for a causal positive influence of schizophrenia risk on lifetime cannabis use.